L Number	Hits	Search Text	DB	Time stamp
1	7	human NEAR mesencephalon	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/28 15:36
7	53	Gage NEAR Fred	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/28 14:52
9	12		USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/28 15:00
14	28	Ray NEAR Jasodhara	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/28 14:56
16	444	mesencephalon	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/28 14:57
17	8		USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/28 14:57
18	225	V-MYC	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/28 15:01
19	25046	TETRACYCLINE	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/28 15:01
20	2	mesencephalon AND V-MYC AND TETRACYCLINE	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/28 15:03
21	18	mesencephalon AND V-MYC	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/28 15:27
22	19509	FGF-2 EGF PDGF GDNF CNTF IGF-1 BDNF	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/28 15:29
23	220	mesencephalon AND (FGF-2 EGF PDGF GDNF CNTF IGF-1 BDNF)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/28 15:29
24	37	mesencephalon AND (FGF-2 EGF PDGF GDNF CNTF IGF-1 BDNF) AND TETRACYCLINE	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/28 15:29
25	115	human SAME mesencephalon	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/28 15:36
27	0	(human SAME mesencephalon) AND (FGF-2 EGF PDGF GDNF CNTF IGF-1 BDNF) AND TETRACYCLINE AND V-MYC	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/28 15:37
26	17	(human SAME mesencephalon) AND (FGF-2 EGF PDGF GDNF CNTF IGF-1 BDNF) AND TETRACYCLINE	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/28 15:55

38	29	(US-6265175-$ or US-6294346-$ or US-6197585-$ or US-6020197-$ or US-6040180-$ or US-6045807-$ or US-6071889-$ or US-5980885-$ or US-5981165-$ or US-6013521-$ or US-5753506-$ or US-5766948-$ or US-5770414-$ or US-5750376-$ or US-5580777-$ or US-5851832-$ or US-6284539-$ or US-5411883-$ or US-5935795-$ or US-6093802-$ or US-6221376-$ or US-6294383-$).did. or (US-20020009743-$ or US-20020039789-$ or US-20020006660-$ or US-20030049234-$ or US-20040009592-$).did. or (WO-9949014-$ or WO-200009669-$).did.	USPAT; US-PGPUB; DERWENT	2004/01/28 15:54
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     (FILE 'HOME' ENTERED AT 16:52:49 ON 28 JAN 2004)

     FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, MEDICONF' ENTERED
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L1          5173 S MESENCEPHALON (L) NEUR?
L2         36018 S IMMORTAL?
L3            35 S L1 (L) L2
L4            16 DUP REM L3 (19 DUPLICATES REMOVED)
L5            16 SORT L4 PY
L6       2865368 S NEUR? OR NERV?
L7          4018 S L6 AND L2
L8          3407 S L6 (L) L2
L9           692 S L8 AND (STEM OR PROGEN? OR MULTIPOTEN? OR PLURI?)
L10           41 S L9 AND TETRA?
L11           17 DUP REM L10 (24 DUPLICATES REMOVED)
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L14           22 S L10 AND V\-MYC
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L16           22 S L15 AND TETRACYCL?
L17           22 S L15 AND TETRACYCLINE
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                 E GAGE F.H./AU
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L24            0 S L22 AND L1
L25          223 S L21 AND L6
L26            6 S L21 AND L9
L27            5 S L22 AND L9

=> d an ti so au ab pi l27 1

L27  ANSWER 1 OF 5  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   1999:672982  CAPLUS
DN   131:269274
TI   PNS cell lines and methods of use therefor
SO   PCT Int. Appl., 84 pp.
     CODEN: PIXXD2
IN   Sah, Dinah W. Y.; Raymon, Heather K.
AB   Conditionally-immortalized PNS progenitor cell lines
     are provided.  Such cell lines, which may be used to
     generate neurons.  The cell lines and/or differentiated cells
     may be used for the development of therapeutic agents to prevent and treat
     a variety of PNS-related diseases.  The cell lines and/or differentiated
     cells may also be used in assays and for the general study of PNS cell
     development, death and abnormalities.
     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
PI   WO 9953028         A1   19991021       WO 1999-US8167   19990414
         W:  AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ,
             DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP,
             KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN,
             MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,
             TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU,
             TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
             ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
             CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     CA 2325603          AA   19991021       CA 1999-2325603  19990414
     AU 9936429          A1   19991101       AU 1999-36429    19990414
     EP 1071750          A1   20010131       EP 1999-918545   19990414
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
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L26 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:176007 CAPLUS
DN 128:229000
TI Development of human CNS cell lines and use to study CNS cell development, death, and abnormalities
SO PCT Int. Appl., 76 pp.
CODEN: PIXXD2
IN Sah, Dinah W. Y.; **Gage, Fred H.**; Ray, Jasodhara
AB Conditionally-**immortalized** human CNS **progenitor** cell lines are provided. Such cell lines, which may be clonal, may be used to generate **neurons** and/or astrocytes. Such cell lines and/or differentiated cells may be used for the development of therapeutic agents to prevent and treat a variety of CNS-related diseases. The cell lines are produced by transfecting CNS **progenitor** cells with oncogenes and growing the cells on polyornithine/laminin, polylysine/laminin, or fibronectin-treated surfaces in culture medium supplemented with proliferation-enhancing factors. Suitable oncogenes include v-myc, N-myc, c-myc, p53, SV40 large T antigen, polyoma large T antigen, E1a adenovirus, and the human papillomavirus E7 protein gene. Such cell lines and/or differentiated cells may also be used in assays and for the general study of CNS cell development, death and abnormalities. Examples of abnormalities include Alzheimer's disease, stroke, traumatic head injuries, and amyotrophic lateral sclerosis.

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9810058	A1	19980312	WO 1997-US15442	19970902
	W: AU, CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9743315	A1	19980326	AU 1997-43315	19970902
	AU 727113	B2	20001130		
	EP 925357	A1	19990630	EP 1997-941398	19970902
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2001500727	T2	20010123	JP 1998-512817	19970902

L26 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:568304 CAPLUS
DN 127:201026
TI Regulatable retroviral vector containing v-myc oncogene for **immortalization** of adult **neuronal progenitor** cells
SO PCT Int. Appl., 42 pp.
CODEN: PIXXD2
IN **Gage, Fred H.**; Ray, Jasodhara; Hoshimaru, Minoru
AB A novel regulatable retroviral vector in which the v-myc oncogene is driven by a tetracycline-controlled transactivator and a human cytomegalovirus minimal promoter fused to tet operator sequence useful for **immortalization** of adult **neuronal progenitor** cells is provided. Producer cell lines which produce high titers of the recombinant retrovirus are also provided. This general method is exemplified by the retroviral vector LINXv-myc. HC2S2 cells from adult rat hippocampus were infected with the retroviral vectors. HC2S2 cells, derived from an **immortalized neuronal progenitor** cell, were differentiated into **neurons** after suppression of the v-myc oncogene.

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9730168	A1	19970821	WO 1997-US2013	19970211
	W: AU, CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 5770414	A	19980623	US 1996-602203	19960220
	CA 2242381	AA	19970821	CA 1997-2242381	19970211
	AU 9722642	A1	19970902	AU 1997-22642	19970211
	AU 721727	B2	20000713		
	EP 892851	A1	19990127	EP 1997-906896	19970211
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2000504584	T2	20000418	JP 1997-529408	19970211

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     AT 16:52:57 ON 28 JAN 2004
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L2         36018 S IMMORTAL?
L3            35 S L1 (L) L2
L4            16 DUP REM L3 (19 DUPLICATES REMOVED)
L5            16 SORT L4 PY
L6       2865368 S NEUR? OR NERV?
L7          4018 S L6 AND L2
L8          3407 S L6 (L) L2
L9           692 S L8 AND (STEM OR PROGEN? OR MULTIPOTEN? OR PLURI?)
L10           41 S L9 AND TETRA?
L11           17 DUP REM L10 (24 DUPLICATES REMOVED)
L12           17 SORT L11 PY
L13            1 S L10 AND C-MYC
L14           22 S L10 AND V\-MYC
L15           22 S L10 AND V-MYC
L16           22 S L15 AND TETRACYCL?
L17           22 S L15 AND TETRACYCLINE
L18           22 FOCUS L17 1-
L19           22 SORT L18 PY
L20            7 DUP REM L19 (15 DUPLICATES REMOVED)
                 E GAGE FRED?/AU
                 E GAGE F.H./AU
L21          279 S E5
                 E SAH DINAH?/AU
L22           25 S E1
L23            3 S L21 AND L1
L24            0 S L22 AND L1
L25          223 S L21 AND L6
L26            6 S L21 AND L9
L27            5 S L22 AND L9

=> d an ti so au ab pi l27 1 3 4 5

L27  ANSWER 1 OF 5  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   1999:672982  CAPLUS
DN   131:269274
TI   PNS cell lines and methods of use therefor
SO   PCT Int. Appl., 84 pp.
     CODEN: PIXXD2
IN   Sah, Dinah W. Y.; Raymon, Heather K.
AB   Conditionally-immortalized PNS progenitor cell lines
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     generate neurons.  The cell lines and/or differentiated cells
     may be used for the development of therapeutic agents to prevent and treat
     a variety of PNS-related diseases.  The cell lines and/or differentiated
     cells may also be used in assays and for the general study of PNS cell
     development, death and abnormalities.
     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
     --------------    ----  --------      ---------------  --------
PI   WO 9953028         A1   19991021      WO 1999-US8167   19990414
         W:  AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ,
             DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP,
             KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN,
             MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,
             TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU,
             TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
             ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
             CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     CA 2325603          AA   19991021      CA 1999-2325603  19990414
     AU 9936429          A1   19991101      AU 1999-36429    19990414
     EP 1071750          A1   20010131      EP 1999-918545   19990414
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
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IE, FI

BR 9909624	A	20010911	BR 1999-9624	19990414
JP 2002511248	T2	20020416	JP 2000-543576	19990414

L27 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:176007 CAPLUS
DN 128:229000
TI Development of human CNS cell lines and use to study CNS cell development, death, and abnormalities
SO PCT Int. Appl., 76 pp.
CODEN: PIXXD2
IN **Sah, Dinah W. Y.**; Gage, Fred H.; Ray, Jasodhara
AB Conditionally-**immortalized** human CNS **progenitor** cell lines are provided. Such cell lines, which may be clonal, may be used to generate **neurons** and/or astrocytes. Such cell lines and/or differentiated cells may be used for the development of therapeutic agents to prevent and treat a variety of CNS-related diseases. The cell lines are produced by transfecting CNS **progenitor** cells with oncogenes and growing the cells on polyornithine/laminin, polylysine/laminin, or fibronectin-treated surfaces in culture medium supplemented with proliferation-enhancing factors. Suitable oncogenes include v-myc, N-myc, c-myc, p53, SV40 large T antigen, polyoma large T antigen, E1a adenovirus, and the human papillomavirus E7 protein gene. Such cell lines and/or differentiated cells may also be used in assays and for the general study of CNS cell development, death and abnormalities. Examples of abnormalities include Alzheimer's disease, stroke, traumatic head injuries, and amyotrophic lateral sclerosis.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9810058	A1	19980312	WO 1997-US15442	19970902
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9743315	A1	19980326	AU 1997-43315	19970902
AU 727113	B2	20001130		
EP 925357	A1	19990630	EP 1997-941398	19970902
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001500727	T2	20010123	JP 1998-512817	19970902

L27 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:371172 CAPLUS
DN 127:93276
TI Bipotent **progenitor** cell lines from the human CNS
SO Nature Biotechnology (1997), 15(6), 574-580
CODEN: NABIF9; ISSN: 1087-0156
AU **Sah, Dinah W. Y.**; Ray, Jasodhara; Gage, Fred H.
AB Human central **nervous** system (CNS) cell lines would substantially facilitate drug discovery and basic research by providing a readily renewable source of human **neurons**. We isolated clonal human CNS cell lines that had been **immortalized** with a tetracycline (Tc)-responsive v-myc oncogene; addn. of Tc to the growth medium suppressed the oncoprotein rapidly and virtually completely, allowing differentiation to proceed. Two classes of bipotent precursor cells were **immortalized**: the first class had a default differentiation pathway of **neurons** only, and the second class had a default differentiation pathway of **neurons** and astrocytes. We found that after exposure to different external signals in vitro, the environment is capable of redirecting the fate of a particular cell, even in the case of the bipotent precursor cell whose default differentiation pathway was **neurons** only. These data suggest that extrinsic cues can prevail over intrinsic determinants in directing cell fate in the human CNS.

L27 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:123431 CAPLUS
DN 124:227790
TI Differentiation of the **immortalized** adult **neuronal progenitor** cell line HC2S2 into **neurons** by regulatable suppression of the v-myc oncogene

SO Proceedings of the National Academy of Sciences of the United States of America (1996), 93(4), 1518-23
CODEN: PNASA6; ISSN: 0027-8424
AU Hoshimaru, Minoru; Ray, Jasodhara; **Sah, Dinah W. Y.**; Gage, Fred H.
AB A regulatable retroviral vector in which the v-myc oncogene is driven by a tetracycline-controlled transactivator and a human cytomegalovirus minimal promoter fused to a tet operator sequence was used for conditional **immortalization** of adult rat **neuronal progenitor** cells. A single clone, HC2S2, was isolated and characterized. Two days after the addn. of tetracycline, the HC2S2 cells stopped proliferating, began to extend **neurites**, and expressed the **neuronal** markers tau, NeuN, **neurofilament** 200 kDa, and glutamic acid decarboxylase in accordance with the reduced prodn. of the v-myc oncoprotein. Differentiated HC2S2 cells expressed large sodium and calcium currents and could fire regenerative action potentials. These results suggest that the suppression of the v-myc oncogene may be sufficient to make proliferating cells exit from cell cycles and induce terminal differentiation. The HC2S2 cells will be valuable for studying the differentiation process of **neurons**.

=> d an ti so au ab pi l26 1 3 4

L26 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:20170 CAPLUS
DN 130:245944
TI The use of neural **progenitor** cells for therapy in the CNS disorders
SO CNS Regeneration (1999), 183-201. Editor(s): Tuszynski, Mark H.; Kordower, Jeffrey H. Publisher: Academic, San Diego, Calif.
CODEN: 67CYA3
AU Ray, Jasodhara; Palmer, Theo D.; Shihabuddin, Lamya S.; **Gage, Fred H.**
AB A review with 84 refs. In recent years a significant no. of **neurol**. diseases have been defined at the mol. level. Somatic gene therapy using genetically modified non-**neuronal** cells expressing therapeutic factors have been successfully used in animal models of **neurodegenerative** diseases. Ability to grow central **nervous** system (CNS)-derived **neural progenitor** cells has proven to be extremely useful to study a diverse phenomenon including the fate choice, differentiation, and synaptic maturation of cells. **Immortal** or perpetual cultures of **neural progenitor** cells implanted into the rodent brain survive, migrate, and integrate in the host cytoarchitecture. These cells can be genetically modified to express therapeutic gene products. The ability of the implanted cells to integrate in the host brain and express transgene products in situ offer potential approaches for gene therapy in certain CNS diseases. The utility of this approach has already been explored in animal models of **neurodegenerative** diseases. This chapter reviews the recent advances made in understanding the nature and potentiality of **neural progenitor** cells in vitro and in vivo as well as their possible use for cell replacement and gene therapy.

L26 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:176007 CAPLUS
DN 128:229000
TI Development of human CNS cell lines and use to study CNS cell development, death, and abnormalities
SO PCT Int. Appl., 76 pp.
CODEN: PIXXD2
IN Sah, Dinah W. Y.; **Gage, Fred H.**; Ray, Jasodhara
AB Conditionally-**immortalized** human CNS **progenitor** cell lines are provided. Such cell lines, which may be clonal, may be used to generate **neurons** and/or astrocytes. Such cell lines and/or differentiated cells may be used for the development of therapeutic agents to prevent and treat a variety of CNS-related diseases. The cell lines are produced by transfecting CNS **progenitor** cells with oncogenes

and growing the cells on polyornithine/laminin, polylysine/laminin, or fibronectin-treated surfaces in culture medium supplemented with proliferation-enhancing factors. Suitable oncogenes include v-myc, N-myc, c-myc, p53, SV40 large T antigen, polyoma large T antigen, E1a adenovirus, and the human papillomavirus E7 protein gene. Such cell lines and/or differentiated cells may also be used in assays and for the general study of CNS cell development, death and abnormalities. Examples of abnormalities include Alzheimer's disease, stroke, traumatic head injuries, and amyotrophic lateral sclerosis.

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9810058	A1	19980312	WO 1997-US15442	19970902
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	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9743315	A1	19980326	AU 1997-43315	19970902
	AU 727113	B2	20001130		
	EP 925357	A1	19990630	EP 1997-941398	19970902
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2001500727	T2	20010123	JP 1998-512817	19970902

L26 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:568304 CAPLUS
DN 127:201026
TI Regulatable retroviral vector containing v-myc oncogene for **immortalization** of adult **neuronal progenitor** cells
SO PCT Int. Appl., 42 pp.
CODEN: PIXXD2
IN **Gage, Fred H.**; Ray, Jasodhara; Hoshimaru, Minoru
AB A novel regulatable retroviral vector in which the v-myc oncogene is driven by a tetracycline-controlled transactivator and a human cytomegalovirus minimal promoter fused to tet operator sequence useful for **immortalization** of adult **neuronal progenitor** cells is provided. Producer cell lines which produce high titers of the recombinant retrovirus are also provided. This general method is exemplified by the retroviral vector LINXv-myc. HC2S2 cells from adult rat hippocampus were infected with the retroviral vectors. HC2S2 cells, derived from an **immortalized neuronal progenitor** cell, were differentiated into **neurons** after suppression of the v-myc oncogene.

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9730168	A1	19970821	WO 1997-US2013	19970211
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	CA 2242381	AA	19970821	CA 1997-2242381	19970211
	AU 9722642	A1	19970902	AU 1997-22642	19970211
	AU 721727	B2	20000713		
	EP 892851	A1	19990127	EP 1997-906896	19970211
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2000504584	T2	20000418	JP 1997-529408	19970211

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(FILE 'HOME' ENTERED AT 16:52:49 ON 28 JAN 2004)

FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, MEDICONF' ENTERED AT 16:52:57 ON 28 JAN 2004

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L2         36018 S IMMORTAL?
L3            35 S L1 (L) L2
L4            16 DUP REM L3 (19 DUPLICATES REMOVED)
L5            16 SORT L4 PY
L6       2865368 S NEUR? OR NERV?
L7          4018 S L6 AND L2
L8          3407 S L6 (L) L2
L9           692 S L8 AND (STEM OR PROGEN? OR MULTIPOTEN? OR PLURI?)
L10           41 S L9 AND TETRA?
L11           17 DUP REM L10 (24 DUPLICATES REMOVED)
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L16           22 S L15 AND TETRACYCL?
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L19           22 SORT L18 PY
L20            7 DUP REM L19 (15 DUPLICATES REMOVED)
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L20 ANSWER 7 OF 7 MEDLINE on STN DUPLICATE 6
AN 96202311 MEDLINE
TI Differentiation of the **immortalized** adult **neuronal progenitor** cell line HC2S2 into **neurons** by regulatable suppression of the **v-myc** oncogene.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1996 Feb 20) 93 (4) 1518-23.
Journal code: 7505876. ISSN: 0027-8424.
AU Hoshimaru M; Ray J; Sah D W; Gage F H
AB A regulatable retroviral vector in which the **v-myc** oncogene is driven by a **tetracycline**-controlled transactivator and a human cytomegalovirus minimal promoter fused to a tet operator sequence was used for conditional **immortalization** of adult rat **neuronal progenitor** cells. A single clone, HC2S2, was isolated and characterized. Two days after the addition of **tetracycline**, the HC2S2 cells stopped proliferating, began to extend **neurites**, and expressed the **neuronal** markers tau, NeuN, **neurofilament** 200 kDa, and glutamic acid decarboxylase in accordance with the reduced production of the **v-myc** oncoprotein. Differentiated HC2S2 cells expressed large sodium and calcium currents and could fire regenerative action potentials. These results suggest that the suppression of the **v-myc** oncogene may be sufficient to make proliferating cells exit from cell cycles and induce terminal differentiation. The HC2S2 cells will be valuable for studying the differentiation process of **neurons**.

L20 ANSWER 6 OF 7 MEDLINE on STN DUPLICATE 5
AN 97325529 MEDLINE
TI Bipotent **progenitor** cell lines from the human CNS.
SO NATURE BIOTECHNOLOGY, (1997 Jun) 15 (6) 574-80.
Journal code: 9604648. ISSN: 1087-0156.
AU Sah D W; Ray J; Gage F H
AB Human central **nervous** system (CNS) cell lines would substantially facilitate drug discovery and basic research by providing a readily renewable source of human **neurons**. We isolated clonal human CNS cell lines that had been **immortalized** with a **tetracycline** (Tc)-responsive **v-myc** oncogene; addition of Tc to the growth medium suppressed the oncoprotein rapidly and virtually completely, allowing differentiation to proceed. Two classes of bipotent precursor cells were **immortalized**: the first class had

a default differentiation pathway of **neurons** only, and the second class had a default differentiation pathway of **neurons** and astrocytes. We found that after exposure to different external signals in vitro, the environment is capable of redirecting the fate of a particular cell, even in the case of the bipotent precursor cell whose default differentiation pathway was **neurons** only. These data suggest that extrinsic cues can prevail over intrinsic determinants in directing cell fate in the human CNS.

L20 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:568304 CAPLUS
DN 127:201026
TI Regulatable retroviral vector containing **v-myc** oncogene for **immortalization** of adult **neuronal progenitor** cells
SO PCT Int. Appl., 42 pp.
CODEN: PIXXD2
IN Gage, Fred H.; Ray, Jasodhara; Hoshimaru, Minoru
AB A novel regulatable retroviral vector in which the **v-myc** oncogene is driven by a **tetracycline**-controlled transactivator and a human cytomegalovirus minimal promoter fused to tet operator sequence useful for **immortalization** of adult **neuronal progenitor** cells is provided. Producer cell lines which produce high titers of the recombinant retrovirus are also provided. This general method is exemplified by the retroviral vector LINXv-myc. HC2S2 cells from adult rat hippocampus were infected with the retroviral vectors. HC2S2 cells, derived from an **immortalized neuronal progenitor** cell, were differentiated into **neurons** after suppression of the **v-myc** oncogene.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9730168	A1	19970821	WO 1997-US2013	19970211
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5770414	A	19980623	US 1996-602203	19960220
CA 2242381	AA	19970821	CA 1997-2242381	19970211
AU 9722642	A1	19970902	AU 1997-22642	19970211
AU 721727	B2	20000713		
EP 892851	A1	19990127	EP 1997-906896	19970211
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2000504584	T2	20000418	JP 1997-529408	19970211

L20 ANSWER 1 OF 7 MEDLINE on STN DUPLICATE 1
AN 2000145994 MEDLINE
TI Motoneuron differentiation of immortalized human spinal cord cell lines.
SO JOURNAL OF NEUROSCIENCE RESEARCH, (2000 Feb 1) 59 (3) 342-52.
Journal code: 7600111. ISSN: 0360-4012.
AU Li R; Thode S; Zhou J; Richard N; Pardinas J; Rao M S; Sah D W
AB Human motoneuron cell lines will be valuable tools for spinal cord research and drug discovery. To create such cell lines, we **immortalized** NCAM(+)/**neurofilament**(+) precursors from human embryonic spinal cord with a **tetracycline** repressible **v-myc** oncogene. Clonal NCAM(+)/**neurofilament**(+) cell lines differentiated exclusively into **neurons** within 1 week. These **neurons** displayed extensive processes, exhibited immunoreactivity for mature **neuron**-specific markers such as tau and synaptophysin, and fired action potentials upon current injection. Moreover, a clonal precursor cell line gave rise to multiple types of spinal cord **neurons**, including ChAT(+)/Lhx3(+)/Lhx4(+) motoneurons and GABA(+) interneurons. These **neuronal** restricted precursor cell lines will expedite the elucidation of molecular mechanisms that regulate the differentiation, maturation and survival of specific subsets of spinal cord **neurons**, and the identification and validation of novel drug targets for motoneuron diseases and spinal cord injury.

L20 ANSWER 3 OF 7 MEDLINE on STN DUPLICATE 3

AN 1998331982 MEDLINE
TI Induction of the N-methyl-D-aspartate receptor subunit 1 in the **immortalized neuronal progenitor** cell line HC2S2 during differentiation into **neurons**.
SO JOURNAL OF NEUROSCIENCE RESEARCH, (1998 Jun 15) 52 (6) 699-708. Journal code: 7600111. ISSN: 0360-4012.
AU Asahi M; Hoshimaru M; Hojo M; Matsuura N; Kikuchi H; Hashimoto N
AB Conditionally **immortalized neuronal progenitor** cell line HC2S2 differentiates into mature **neurons** after suppression of the **v-myc** expression with **tetracycline**. Reverse transcription-polymerase chain reaction analyses were used to measure expression levels of N-metyl-D-aspartate receptor subunit 1 (NMDAR1) mRNAs encoding splice variants (NMDAR1a, -exon 5; NMDAR1b, +exon 5) in HC2S2 cells during the differentiation. Differential induction of NMDAR1a and NMDAR1b mRNAs was observed during the differentiation. Very low expression of NMDAR1 was observed in undifferentiated HC2S2 cells. NMDAR1a mRNA was induced coincidentally with the emergence of **neurites**, whereas NMDAR1b mRNA was induced at the time of network formation. Immunohistochemistry also demonstrated induction of NMDAR1 immunoreactivity in differentiated HC2S2 cells. In addition, expression of NMDAR2 mRNA and immunoreactivity was observed in undifferentiated and differentiated HC2S2 cells, suggesting that functional NMDA receptors are present in differentiated HC2S2 cells. While exposure to NMDA resulted in almost no cell death in undifferentiated HC2S2 cells, NMDA induced cell death in differentiated HC2S2 cells in a dose-dependent fashion. These findings suggest that the expression of NMDAR1 mRNA may be regulated by myc or its counterpart during **neuronal** terminal differentiation and that the splicing choice between NMDAR1a and NMDAR1b may vary according to the formation of **neuronal** network.

L20 ANSWER 2 OF 7 MEDLINE on STN DUPLICATE 2
AN 1999307333 MEDLINE
TI **Immortalized** human dorsal root ganglion cells differentiate into **neurons** with nociceptive properties.
SO JOURNAL OF NEUROSCIENCE, (1999 Jul 1) 19 (13) 5420-8. Journal code: 8102140. ISSN: 0270-6474.
AU Raymon H K; Thode S; Zhou J; Friedman G C; Pardinas J R; Barrere C; Johnson R M; Sah D W
AB A renewable source of human sensory **neurons** would greatly facilitate basic research and drug development. We had established previously conditionally **immortalized** human CNS cell lines that can differentiate into functional **neurons** (). We report here the development of an **immortalized** human dorsal root ganglion (DRG) clonal cell line, HD10.6, with a **tetracycline**-regulatable **v-myc** oncogene. In the proliferative condition, HD10.6 cells have a doubling time of 1.2 d and exhibit a **neuronal** precursor morphology. After differentiation of clone HD10.6 for 7 d in the presence of **tetracycline**, **v-myc** expression was suppressed, and >50% of the cells exhibited typical **neuronal** morphology, stained positively for **neuronal** cytoskeletal markers, and fired action potentials in response to current injection. Furthermore, this cell line was fate-restricted to a **neuronal** phenotype; even in culture conditions that promote Schwann cell or smooth muscle differentiation of **neural** crest **stem** cells, HD10.6 differentiated exclusively into **neurons** . Moreover, differentiated HD10.6 cells expressed sensory **neuron** -associated transcription factors and exhibited capsaicin sensitivity. Taken together, these data indicate that we have established an **immortalized** human DRG cell line that can differentiate into sensory **neurons** with nociceptive properties. The cell line HD10.6 represents the first example of a human sensory **neuronal** line and will be valuable for basic research, as well as for the discovery of novel drug targets and clinical candidates.

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L5 ANSWER 10 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN

SEARCH HISTORY

AN 2000:133811 CAPLUS
DN 132:177726
TI Human mesencephalon cell lines and methods of use therefor
SO PCT Int. Appl., 28 pp.
CODEN: PIXXD2
IN Sah, Dinah W.; Raymon, Heather K.
AB Conditionally-**immortalized** human **mesencephalon** cell lines are provided. Such cell lines, which may be clonal, may be used to generate **neurons**, including dopaminergic **neurons**. The cell lines and/or differentiated cells may be used for the development of therapeutic agents to prevent and treat a variety of **neurol**. diseases such as Parkinson's disease. The cell lines and/or differentiated cells may also be used in assays and for the general study of **mesencephalon** cell development and differentiation.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000009669	A1	20000224	WO 1999-US18403	19990812
W: AU, CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2340060	AA	20000224	CA 1999-2340060	19990812
AU 9954825	A1	20000306	AU 1999-54825	19990812
EP 1105464	A1	20010613	EP 1999-941107	19990812
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002522070	T2	20020723	JP 2000-565106	19990812

L5 ANSWER 2 OF 16 MEDLINE on STN
AN 96429942 MEDLINE
TI Evidence for a novel neurotrophic factor for dopaminergic neurons secreted from mesencephalic glial cell lines.
SO JOURNAL OF NEUROSCIENCE RESEARCH, (1996 Mar 1) 43 (5) 576-86.
Journal code: 7600111. ISSN: 0360-4012.
AU Engele J; Rieck H; Choi-Lundberg D; Bohn M C
AB Our previous studies have shown that primary mesencephalic glia secrete factors that promote dopaminergic cell survival and differentiation in vitro. To obtain enough starting material to identify the **neurotrophic** activity, embryonic day (E)14.5 rat mesencephalic glia were stimulated with acidic fibroblast growth factor to increase number of cells. These cells were replated in the absence of **neurons** and **immortalized** by transfection with the SV 40 large T-antigen. Clonal cell lines were established and characterized for immunoreactivity (IR) to various glial and non-glial markers. Media conditioned by these cell lines were tested for survival-promoting effects on dopaminergic **neurons** in serum-free cultures of the dissociated E14.5 rat **mesencephalon**. All cell lines expressed IR for the astrocytic marker, GFAP, the oligodendroglial marker, CNP, and for A2B5, a marker for O-2A progenitor cells, but were negative for the **neuronal** marker, microtubule associated protein-2, and the fibroblast marker, fibronectin. Moreover, treatment of serum-free cultures of the dissociated E14.5 **mesencephalon** with glial cell line-CM conditioned medium (CM) delayed dopaminergic cell death in a dose-dependent manner, resulting in a maximal twofold to sixfold increase in the number of surviving tyrosine hydroxylase-IR **neurons** at various days in vitro. This increase in dopaminergic cell survival was not mimicked by GDNF, BDNF or NT-3 within the initial 3 days of cultivation. Moreover, initial biochemical characterization demonstrated that the **neurotrophic** activity is restricted to the high MW fraction of >50 kD of glial cell line-CM. Since the apparent MW of this factor exceeds the size of most known growth factors, it may represent a novel dopaminergic **neurotrophic** factor.

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